(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
10 May 2002 (10.05.2002)

PCT

(10) International Publication Number
WO 02/36007 A1

(51) International Patent Classification[7]: A61B 5/07

(21) International Application Number: PCT/US01/32420

(22) International Filing Date: 17 October 2001 (17.10.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/702,941 30 October 2000 (30.10.2000) US

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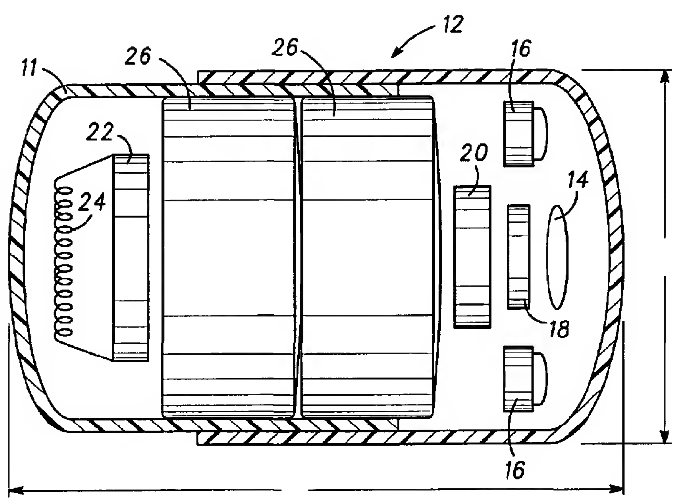
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,

[Continued on next page]

(54) Title: INGESTIBLE CAPSULE VIDEO TRANSMITTING FLUORESCENT IMAGES



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(57) Abstract: An improved and novel ingestible capsule (10) and method for determining medical information from within the alimentary canal of a human or an animal utilizing an ingestible capsule including a non-digestible outer shell (11). Housed within the outer shell are a lens (14), an illuminating LED (16), a filter (18), an imager (20), a transmitter (22), an antenna (24), and a miniature battery (26), the LED, and transmitter.An improved method for obtaining diagnostic medical information including the steps of ingesting (32) a fluorescent dye, such as an antibody-labeled fluorescent dye material, thereby tagging an area of interest, ingesting (34) a rinsing liquid to wash away non-specific fluorescent dye, and ingesting a capsule (36), characterized as illuminating and imaging the fluorescent tagged area of interest. Once images are received, a low frequency transmitter, powered by a miniature battery, sends (40) a video signal to outside the body to a receiver. The transmitted signal provides for images of the tagged area of interest.

WO 02/36007 A1

CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

INGESTIBLE CAPSULE VIDEO TRANSMITTING FLUORESCENT IMAGES

Field of the Invention

The present invention relates to a novel ingestible capsule for use in the field of medicine and method of using the capsule for the accumulation of medical data from within the body of animals, and in particular humans.

Background of the Invention

It is highly desirable to obtain certain medical information and detect certain medical diseases, in particular cancer, without the painful invasive procedures currently used in the medical field. Many of these procedures are unduly stressful and in extreme cases, deter the patient from seeking medical assistance and initial diagnosis. Invasive procedures, or those medical procedures which require the entering of a part of the body, as by incision, scope, etc., are commonly utilized to diagnosis certain diseases and includes procedures such as those utilizing needles, flexible tubes, endoscopic procedures, and surgical procedures.

Many of these diagnostic procedures rely upon the specific procedure or device utilized and the skill of the operator of the device or the one performing the procedure. One such procedure that is typically used today as a common diagnostic tool is colonoscopy for the detection of colorectal cancer (CRC). A colonoscopy generally includes direct visual examination of the colon, ileocecal value, and portions of the terminal ileum by means of a fiberoptic endoscope. A colonoscopy is typically performed by a qualified gastroenterologist. During a colonoscopy the patient is generally awake but sedated. During the procedure a flexible endoscope is inserted in rectum and advanced through the various portions of the lower GI tract. Important anatomic landmarks are identified and surfaces are examined for ulcerations, polyps, hemorrhagic sites, neoplasms, strictures, etc. Dependent upon identified conditions, colorectal cancer, or precancerous conditions of the colon are diagnosed. In many instances, of this invasive procedure, complications arise. The most common complication being perforation of the colon in which diagnosis may be delayed for days until an infection is present. Perforation may be caused by mechanical trauma from the instrument tip, especially if the wall is weakened. Less commonly, perforation may be non-instrumental, secondary to aggressive insufflation with air. However, serious complications from perforation have

been reported in routine cases. In addition, hemorrhaging can arise as a complication and many times requires repeat colonoscopy to coagulate the bleeding. In a few instances angiography and surgery have been required. A third less common complication is respiratory depression, which is usually due to oversedation in the patient with chronic lung disease.

Other common diagnostic procedures include digital rectal exams, fecal occult blood tests (FOBT) utilizing stool samples, barium enema x-rays, and endoscopic sigmoidoscopy. These procedures are all utilized to diagnose cancerous conditions. During an endoscopic sigmoidoscopy, direct examination of the rectum, sigmoid colon, and proximal portions of the colon (60 cm) is achieved by means of a flexible fiberoptic endoscope. The procedure is generally performed in a physician's office with minimal bowel preparation. The 35 cm scope is more comfortable and less expensive than its larger counterpart, the colonoscopy. Although, the yield of this instrument is somewhat less, with only 40% of malignant or premalignant colonic lesions diagnosed.

All of these procedures are termed invasive procedures and can cause high level of discomfort for the patient. Therefore it is desirable to have a non-invasive procedure that can detect diseases, and/or conditions, such as cancer or the like in their very early stages.

In addition, the medical community has recognized a need for more reliable and less invasive procedures for the detection and thus diagnosis of medical diseases. In recent years "radio pills" have come into being. These pills provide for a means to monitor bodily factors and can either be implanted or ingested and provide for the transmission of information outside of the body. Many of these devices have been quite cumbersome in receiving means, as well as unreliable and generally do not provide for determination of the geographic location of the pill.

Many cancer detection means are known in the medical field, one of such is the use of cancer markers. In order to develop a successful screening procedure for detection of various diseases, including cancer, identification of appropriate and reliable diagnostic markers is essential. There are typically three (3) general categories of such markers: physical, genetic and chemical. One such procedure currently being utilized in the medical field to detect early stages of pre-colon cancer polyp development, is the physical characterization of inner surfaces of the intestine using the endoscopy imaging techniques, such as those previously described with respect to colonoscopy, and flexible sigmoidoscopy and in-vivo imaging capsules.

Endoscopy and in-vivo imaging capsule techniques rely on the examination of physical appearance of the gastrointestinal tract for diagnosis, and thus lack the

specificity and sensitivity provided by the inclusion of a biochemical sensor. In addition, endoscopy, colonoscopy and in-vivo imaging capsules as we know them today rely on the illumination of the alimentary canal solely for imaging purposes. As previously stated the advancement of cancer research and molecular biology has provided us with identified cancer specific markers. One method of utilizing these specific markers is based on the highly specific antigen/antibody interaction. It has been found that the specificity of the diagnosis resulting from antibody/antigen interaction can not be matched by any type of physical appearance evaluation. Therefore, chemical detection means are the most logical to pursue for in-vivo mode of detection. Thus, the combination of chemical detection with illuminated imaging would provide for an enhanced method of detection.

Accordingly, it is an object of the present invention to provide for a device for the detecting and diagnosing of medical conditions utilizing chemical markers in combination with in-vivo imaging capsules.

It is another object of the present invention to provide for a device that is ingestible, such as a capsule, that can transmit diagnostic information to a remote receiver, positioned external to the body, that is reactive upon the imaging of a predetermined factor according to the diagnostic marker utilized.

It is yet another purpose of the present invention to provide for a process of receiving information and diagnosing medical conditions by introducing an ingestible capsule into the body, which is capable of transmitting perceived information based upon detection of a predetermined condition utilizing a chemical marker and in-vivo imaging.

Summary of the Invention

These needs and others are substantially met through provision of an ingestible capsule for determining medical information from within the alimentary canal of a human or an animal including a non-digestible outer shell that is configured to pass through the alimentary canal. Housed within the outer shell are a lens, an illuminating LED, a filter, a CMOS imager, a transmitter, an antenna, and a miniature battery for powering the imager, the LED, and transmitter.

In addition, disclosed is a method for obtaining diagnostic medical information including the steps of ingesting a fluorescent dye, such as an antibody-labeled fluorescent dye, thereby tagging predetermined target tissue, ingesting a rinsing liquid to wash away non-specific fluorescent dye, and ingesting a capsule, characterized as illuminating and imaging the

predetermined target tissue. Once images are received, a low frequency transmitter, powered by a miniature battery, sends a signal to outside the body to a receiver. The transmitted signal provides for images of predetermined target tissue.

Brief Description of the Drawings

The foregoing and further and more specific objects and advantages of the instant invention will become readily apparent to those skilled in the art from the following detailed description of a preferred embodiment thereof taken in conjunction with the drawings, in which:

FIG. 1 illustrates a cross-sectional view of an ingestible capsule according to the present invention; and

FIG. 2 illustrates a simplified schematic circuit diagram of the ingestible capsule according to the present invention.

Detailed Description of the Preferred Embodiments

During the course of this description, like numbers are used to identify like elements according to the different figures that illustrate the invention.

Accordingly, FIG. 1 illustrates in simplified cross-sectional view an ingestible capsule according to the present invention. More specifically, illustrated in FIG.1, is an ingestible capsule, designated 10 and the manner in which the components housed with ingestible capsule 10 are interrelated in general. Ingestible capsule 10 typically comprises an optical dome 12, a lens 14, at least one illuminating LED 16, a filter 18, a CMOS imager 20, a transmitter 22, an antenna 24, and a power source 26, such as a miniature battery power source. Components 12, 14, 16, 18, 20 and 22 are interrelated to provide for the detection of a predetermined factor or condition, such as the presence of an enzyme, antigen, antibody, specific pH level, or the like.

Illustrated in a schematic flow diagram, referenced FIG. 2, are steps 30 included in the method of obtaining diagnostic medical information from within the alimentary canal of a human or animal according to the present invention. During typical operation, and as illustrated in FIG. 2, when taken in light of the teachings of FIG. 1, initially a chemical dye material, more specifically an ingestible fluorescent dye, such as an antibody-labeled dye, is ingested 32 by the patient. Next, a fluorescent rinsing liquid is ingested 34 by the patient to wash away any non-specific fluorescent dye. This process provide for the dye labeling of specific tissue, that is pre-identified by the ingestion 32 of the

chemical dye material, more particularly the fluorescent dye. Next, ingestible capsule 10 is swallowed 36 by the patient similar to a conventional pill/capsule and propelled through the alimentary canal by natural contractions, called peristalsis. This propelling of capsule 10 through the alimentary canal provides for the collection 38 of image data. Illuminating LEDs 16 are fabricated to illuminate the alimentary canal, through the optical dome 12. Illuminating LEDs 16 provide the light to illuminate the inner walls of the alimentary canal as the capsule 10 passes therethrough. Lens 14 provides for the focusing of the light emitted from illuminating LEDs 16, back onto the imager 20. Filter 18 provides for the blocking out of excitation light and allow for the transmission of emitted fluorescent light from dye labeled tissue. Filter 18 serves to detect a fluorescence signal from the dye labeled tissue notifying imager 20 to respond.

Due to the ingestion of fluorescent dye 32 which is attracted to predetermined condition, an image of this tissue can be received by imager 20. Thus there exists the ability to detect the presence of a specific condition, such as a level of enzyme, antigen, antibody, pH, etc. Low frequency transmitter 22 is then switched on upon the receipt of image data and is characterized as sending 40 a signal of the images to a receiver positioned outside the body. This presence of

fluorescent labeled tissue which is imaged, means the presence of a predetermined factor or condition. Subsequently, capsule 10 is passed through the alimentary canal and exits the body, while image data is received and interpreted by medical professionals 42.

Referring again to FIG. 1, capsule 10 is fabricated small enough to be easily swallowed by a human or animal. Typically capsule 10 is fabricated to be approximately 30 mm as illustrated by reference X, by less than approximately 11mm as illustrated by reference Y. More specifically, capsule 10 is approximately less than 1" long, by less than ½" wide and is fabricated of a sealed, non-digestible outer shell 11 that is shaped so as to easily pass through the alimentary canal. Capsule 10 does not include any external wires, fibers, optical bundles or cables, although it is anticipated that capsule 10 can additionally include further optical components, etc., to further aid in diagnosing. As previously stated, capsule 10 is propelled by peristalsis, or natural contractions, through the alimentary canal, or gastrointestinal tract, and does not require any pushing force to propel it through the bowel.

The premise for operation of capsule 10 is biosensing in conjunction with fluorescence imaging. Typically biosensing involves the use of biological materials, such as enzymes, cells, antibodies, antigens,

or the like, that interact in some manner when the biological material (receptor) comes into contact with the substance of interest in the tested sample. In the manner of using capsule 10 of the present invention, a fluorescent dye 32, and more particularly an antibody-labeled fluorescent dye, is utilized to detect and mark the existence of certain pre-identified condition or material. The step of ingesting an antibody-labeled fluorescent dye 32 provides for diagnosis of a specific condition, such as that indicative of a cancer precursor.

It is disclosed that in the preferred embodiment, an antibody-labeled fluorescent dye material is utilized, such as a semiconductor nanocrystal dye, for the purpose of in vivo labeling and serving as a staining agent for in-vivo fluorescence detection. Nanocrystal dyes can be made from different kinds of semiconductor material. Compared to organic dyes, nanocrystal dyes have several unique characters and advantages. First, the size and in some cases the shape of the nanocrystal particles can be controlled during manufacture. It is anticipated that in some instances, the size of the nanoparticles can be tailored to suit specific applications, more particularly, the size of the particles can be fabricated to either penetrate or not penetrate a particular cell. Second, emission wavelength of the nanocrystal is size dependent, therefore by monitoring the emission wavelength of the nanocrystal, one can tell the size of

the nanoparticles. Thirdly, any light with a wavelength shorter than the nanoparticle's emission wavelength will contribute to its excitation. Therefore nanocrystal dyes, have a better excitation efficiency compared to that of organic dyes. Fourth, nanocrystal dyes are more photostable than organic dyes.

In addition to cancer cells, or cancer precursor cells, these fluorescent nanoparticles or dyes 32, can be used to label other cell types. For example, the fluorescent nanoparticles can be used to selectively label muscle cells from a mixture of fibroblast cells, epithelial cells, etc. This has great implications for disease diagnostics in that any organ/structure of a human or animal consists of a mixture of cell types. In many cases, the abnormality of particular cell types has to be known before correct diagnostics. The advantage of cell labeling by nanoparticles can improve many traditional biological assays, such as apoptosis assay, immunological assays and in situ hybridization.

In this particular invention, the fluorescent nanocrystals are used in-vivo and are imaged by ingestible capsule 10. As previously described with reference to FIG. 2, specific antibody or chemical tagged semiconductor nanocrystal dyes are ingested 32 and thus delivered to the alimentary canal. In the presence of cancer tissue, specific antibodies, or chemicals, the fluorescent nanocrystal dyes are deposited either on a

surface of the cancer tissue or actually penetrate into the cancer cell to stain the cell components. The unbonded nanocrystal dyes are then washed away by the ingesting of a rinsing agent 34. Next, the patient ingests 36 capsule 10. Capsule 10 travels through the alimentary canal and collects imaged data 38. The fluorescent tagged cancer tissue is detected by capsule 10, by imaging the fluorescent matter. This image data is transmitted 40 via transmitter 22 to a remotely positioned receiver. Sensing capsule 10 is ultimately passed 42 through the alimentary canal and exits the body. Image data provided by imager 22, is received by a remote receiver and interpreted by a medical professional 42 for diagnosis.

It should be understood that it is anticipated by this disclosure that numerous fluorescent dye materials 32, including antibody-labeled fluorescent dye materials, are utilized with differing marker properties, thereby serving as a diagnostic tool for a plurality of conditions, simultaneously. Additionally, a positioning indicator (not shown) can optionally be included for the purpose of determining the exact position of the capsule 10 at any given time in the alimentary canal.

Thus, an ingestible capsule including a small power source, such as a battery, a filtering means and an imager for the purpose of obtaining images of fluorescent tagged tissue is disclosed. The transmitter emits a

signal to an externally located receiver as it travels through the alimentary canal, thereby providing for images of an identified predetermined substance of interest.

What is claimed is:

1. An ingestible capsule for determining medical information from within the alimentary canal of a human or an animal comprising:

a non-digestible outer shell that is configured to pass through the alimentary canal, the non-digestible outer shell housing within;

an imager;

a lens system for imaging a chemically tagged area of interest onto the imager;

an illuminating LED for providing illumination to the area of tissue;

a filter for blocking out excitation light emitted by the illuminating LED;

a low frequency transmitter for providing a signal and thus an image of the chemically tagged area of tissue to outside the body; and

a power source for powering the imager, the LED, and transmitter.

2. An ingestible capsule for determining medical information in the body of a human or an animal as claimed in claim 1 wherein the chemically tagged area of tissue is tagged with a chemical dye material.

3. An ingestible capsule for determining medical information in the body of a human or an animal as claimed in claim 2 wherein the chemical dye material reacts to a pre-identified condition, characterized as a level of enzyme, antigen, or antibody.

4. An ingestible capsule for determining medical information in the body of a human or an animal as claimed in claim 2 wherein the chemical dye material is a fluorescent dye material.

5. An ingestible capsule for determining medical information in the body of a human or an animal as claimed in claim 4 wherein the fluorescent dye material is an antibody-labeled fluorescent dye material.

6. An ingestible capsule for determining medical information in the body of a human or an animal as claimed in claim 4 wherein the fluorescent dye material is a semiconductor nanocrystal dye.

7. An ingestible capsule for determining medical information in the body of a human or an animal as claimed in claim 1 wherein the power source is a miniature battery.

8. An ingestible capsule for determining medical information in the body of a human or an animal as claimed in claim 1 wherein the transmitter is a miniature transmitter formed on a ceramic or a plastic material.

9. An ingestible capsule for determining medical information in the body of a human or an animal as claimed in claim 1 wherein the transmitter emits a video signal to an externally remote receiver.

10. A method for obtaining diagnostic medical information from within the alimentary canal of a human or an animal comprising the steps of:

ingesting a chemical dye material into the alimentary canal;

ingesting a in-vivo imaging capsule including an imager, a lens system for imaging a chemically tagged area of interest onto the imager, an illuminating LED for providing illumination to the tagged area of interest, a filter for blocking out excitation light emitted by the illuminating LED, a low frequency transmitter for providing a signal and thus an image of the chemically tagged area of interest to outside the body, and a power source for powering the imager, the LED, and transmitter; and

remotely positioning a receiver characterized as receiving the signal from the transmitter.

11. A method for obtaining diagnostic medical information from within the alimentary canal of a human or an animal as claimed in claim 10 further including the step of ingesting a rinsing liquid prior to ingesting the in-vivo imaging capsule, the ingesting of the rinsing liquid characterized as washing away any non-specific chemical dye material.

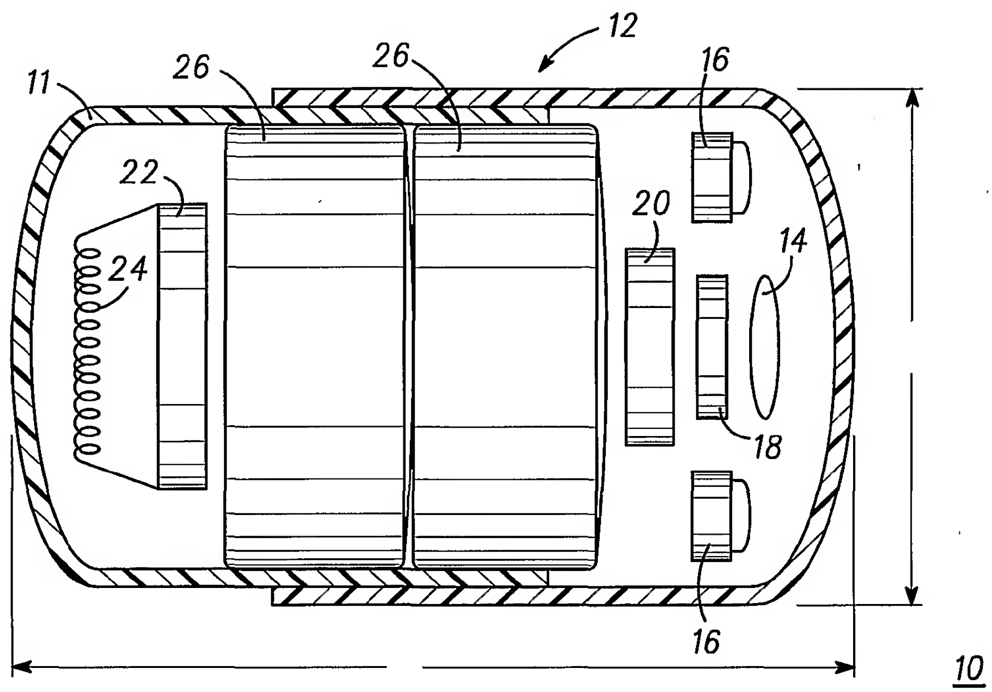

FIG. 1

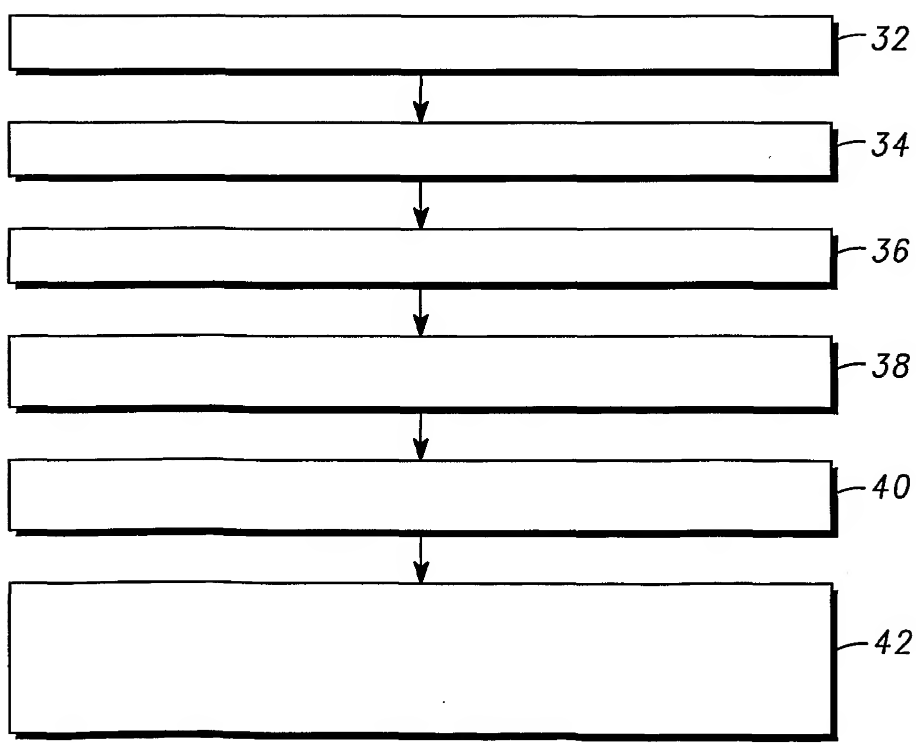

FIG. 2

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/32420

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/07

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 278 077 A (MIZUMOTO MORIHIDE) 14 July 1981 (1981-07-14) summary of the invention	1
A	EP 0 667 115 A (ISRAEL STATE) 16 August 1995 (1995-08-16) summary of the invention	1
A,P	WO 01 50941 A (REFAEL MOSHE) 19 July 2001 (2001-07-19) brief decription of the invention	1
A,P	US 6 240 312 B1 (HO PING PEI ET AL) 29 May 2001 (2001-05-29)	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

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"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 February 2002	05/03/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Papone, F

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 01/32420

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